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ACUTE EXPOSURE GUIDELINE LEVELS (AEGLs) FOR BENZONITRILE

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Mechanism of Toxicity

Unlike the other nitriles considered, cyanide IS NOT a metabolite of benzonitrile.

No information regarding the mechanism of toxicity of benzonitrile was located.

Symptoms of acute poisoning are similar to those produced by other uncoupling agents, such as pentachlorophenol and dinitrophenol:

> **Fatigue, excessive sweating, thirst, pyrexia, anxiety, tachycardia, and hyperventilation**

Rat and mouse data have suggested signs of narcosis

AEGL-1 VALUES: BENZONITRILE				
10 minute	30 minute	1 hour	4 hour	8 hour
19 ppm	19 ppm	15 ppm	3.8 ppm	2.0 ppm

Species: Rat (6 males/group)
Concentration: 900 ppm
Time: 1-hour
Endpoint: Irritation of extremities
Reference: MacEwen and Vernot, 1974

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 30-minute time period, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001). The 30-minute AEGL-1 was also adopted as the 10-minute value.

Uncertainty Factors:

Interspecies = 10 The rat is not the most sensitive species

Intraspecies = 3 Steep concentration-response curve implies little individual variability.

Mice exposed via inhalation (10% mortality for mice exposed to 890 ppm for 2 hr [ct = 1780 ppm·hr] vs. 100% mortality for mice exposed to 700 ppm for 4 hr [ct = 2800 ppm·hr] (MacEwen and Vernot, 1974).

Rats exposed orally (0.6 g/kg, 0/4 deaths vs. 2.0 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Rabbits exposed dermally (0.9 g/kg, 0/4 deaths vs. 1.4 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Modifying Factor = 2 Sparse data base and potential delayed hepatic effects, such as the hepatic congestion evidenced in mice (MacEwen and Vernot, 1974)

AEGL-2 VALUES: BENZONITRILE				
10 minute	30 minute	1 hour	4 hour	8 hour
27 ppm	27 ppm	22 ppm	12 ppm	5.5 ppm

Species: Rat (6 males/group)
Concentration: 900 ppm
Time: 3-hour
Endpoint: Labored breathing; poor coordination
Reference: MacEwen and Vernot, 1974

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 30-minute and 1-hour time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001). The 30-minute AEGL-2 was also adopted as the 10-minute value.

Uncertainty Factors:

Interspecies = 10 The rat is not the most sensitive species

Intraspecies = 3 Steep concentration-response curve implies little individual variability.

Mice exposed via inhalation (10% mortality for mice exposed to 890 ppm for 2 hr [ct = 1780 ppm·hr] vs. 100% mortality for mice exposed to 700 ppm for 4 hr [ct = 2800 ppm·hr] (MacEwen and Vernot, 1974).

Rats exposed orally (0.6 g/kg, 0/4 deaths vs. 2.0 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Rabbits exposed dermally (0.9 g/kg, 0/4 deaths vs. 1.4 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Modifying Factor = 2 Sparse data base and potential delayed hepatic effects, such as the hepatic congestion evidenced in mice (MacEwen and Vernot, 1974)

AEGL-3 VALUES: BENZONITRILE				
10 minute	30 minute	1 hour	4 hour	8 hour
71 ppm	71 ppm	56 ppm	23 ppm	11 ppm

Species: Mouse (10 males/group)
Concentration: 890 ppm
Time: 2-hours
Endpoint: 10% Mortality (1/10)
Reference: MacEwen and Vernot, 1974

Time Scaling: $C^n \times t = k$, where $n = 3$ for the 30-minute and 1-hour time periods, and $n = 1$ for the 4- and 8-hour time periods, to provide AEGL values that would be protective of human health (NRC, 2001). The 30-minute AEGL-3 was also adopted as the 10-minute value.

Uncertainty Factors:

Interspecies = 3 The mouse is the most sensitive species

Intraspecies = 3 Steep concentration-response curve implies little individual variability.

Mice exposed via inhalation (10% mortality for mice exposed to 890 ppm for 2 hr [ct = 1780 ppm·hr] vs. 100% mortality for mice exposed to 700 ppm for 4 hr [ct = 2800 ppm·hr] (MacEwen and Vernot, 1974).

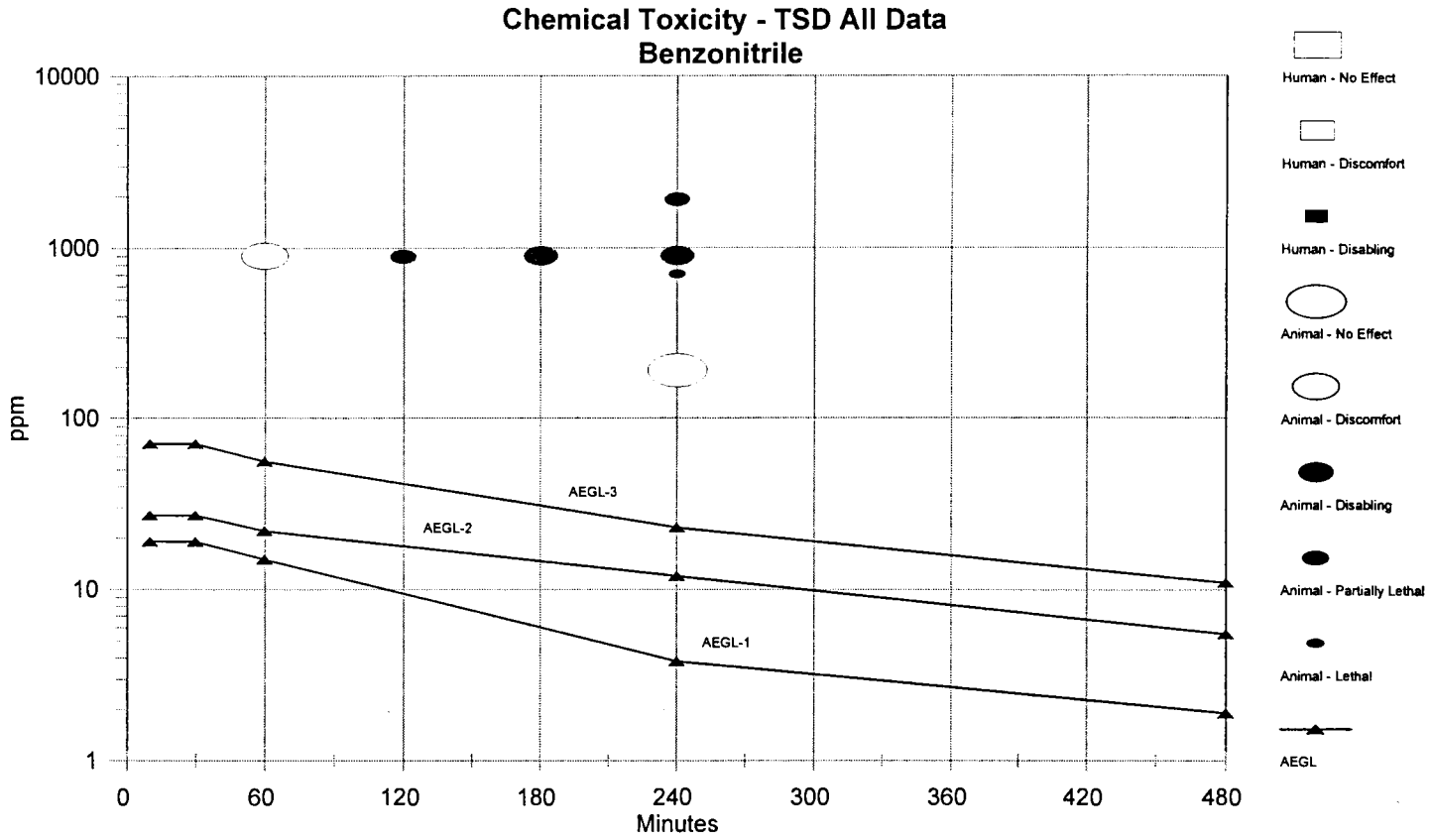
Rats exposed orally (0.6 g/kg, 0/4 deaths vs. 2.0 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Rabbits exposed dermally (0.9 g/kg, 0/4 deaths vs. 1.4 g/kg, 4/4 deaths) (Industrial Bio-Test, 1970).

Modifying Factor = 2 Endpoint where 1/10 mice died; Sparse data base and potential delayed hepatic effects, such as the hepatic congestion evidenced in mice

THERE ARE NO OTHER EXTANT STANDARDS AND GUIDELINES FOR BENZONITRILE!

Summary of Proposed AEGL Values for Benzonitrile					
Guideline	Exposure Duration				
	10-minutes	30-minutes	1-hour	4-hours	8-hours
AEGL-1	19 ppm	19 ppm	15 ppm	3.8 ppm	2.0 ppm
AEGL-2	27 ppm	27 ppm	22 ppm	12 ppm	5.5 ppm
AEGL-3	71 ppm	71 ppm	56 ppm	23 ppm	11 ppm


Chemical Toxicity - TSD All Data
Benzonitrile
10000
1000
100
10
1
ppm
0
60
120
180
240
300
360
420
480
Minutes
AEGL-3
AEGL-2
AEGL-1
Human - No Effect
Human - Discomfort
Human - Disabling
Animal - No Effect
Animal - Discomfort
Animal - Disabling
Animal - Partially Lethal
Animal - Lethal
AEGL